# Left Ventricular Wall Motion Response to Intravenous Propranolol

*By* SAMUEL J. SHUBROOKS, JR., M.D., LEONARD M. ZIR, M.D., ROBERT E. DINSMORE, M.D., AND J. WARREN HARTHORNE, M.D.

SUMMARY

The effects of intravenous propranolol on left ventricular wall motion and hemodynamics were studied in 16 patients, 12 with significant coronary artery disease and four with chest pain but no coronary disease. Eight patients received 0.10 mg/kg and eight received 0.15 mg/kg of propranolol intravenously. All underwent atrial pacing at a constant rate. Left ventricular angiograms were performed before and 20 minutes after propranolol. At both doses, propranolol caused no significant change in left ventricular systolic or diastolic pressures, either before or immediately following ventriculography. Cardiac index fell significantly ($3.4 \pm 0.2$ [SEM] to $2.6 \pm 0.1$ L/min/m$^2$) with the higher dose only. Of the ten patients with coronary artery disease and adequate ventriculograms, one patient had a normal left ventricle, two had regional hypokinesis, only three had areas of hypokinesis and akinesis, two had dyskinetic and akinetic areas, and two had areas of hypokinesis, akinesis and dyskinesis. No changes in regional contractility occurred with propranolol except for a minimal increase in hypokinesis in one patient at each dosage and equivocal development of a new area of slight hypokinesis in one patient and minimal apex dyskinesis in another at the higher dosage. Of the four patients without coronary artery disease, two were affected by propranolol, one with initial regional akinesis and dyskinesis had slight worsening with propranolol and one with regional hypokinesis developed a definite new area of hypokinesis. Therefore, propranolol, even in large intravenous doses, resulted in no significant change in left ventricular wall motion in patients with coronary artery disease.

**Additional Indexing Words:**

Cardiac catheterization  Coronary artery disease  Left ventricular contractility



PROPRANOLOL IS COMMONLY USED for the treatment of angina pectoris, exerting its beneficial effects at least in part by decreasing myocardial contractility and thereby oxygen consumption. Although left ventricular contraction abnormalities are common in patients with previous myocardial infarction,[1] the influence of propranolol on such wall motion abnormalities has not been adequately studied. Creation of new areas of asynergy, or worsening of existing areas, particularly of dyskinetic segments, in patients with previously impaired cardiac function, may critically exacerbate myocardial ischemia and failure. If, however, the decrease in contractility with propranolol results in a reduction in abnormal systolic movement of dyskinetic areas, as has been recently suggested,[2] propranolol may actually improve myocardial function. In the only reported angiographic study of the effects of propranolol on left ventricular wall motion,[3] it has been said that in ten patients, only four of whom had coronary artery disease, propranolol resulted in the frequent occurrence of new areas of left ventricular asynergy or significant accentuation of pre-existing areas. The present study was designed to further evaluate the effects of propranolol on hemodynamics and on left ventricular wall motion in patients with coronary artery disease.

From the Cardiac Unit of the General Medical Service and the Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

Supported in part by USPHS Grant HL 5196 (Training Grant).

Dr. Shubrooks' present address is Cardiology Unit, New England Deaconess Hospital, Boston, Massachusetts 02215.

Address for reprints: Leonard M. Zir, M.D., Cardiac Catheterization Laboratory, Massachusetts General Hospital, Fruit Street, Boston, Massachusetts 02114.

Received October 15, 1974; revision accepted for publication February 6, 1975.

## Methods

Sixteen patients were selected from those undergoing diagnostic coronary angiography for suspected coronary artery disease. It was intended to study patients with varying degrees of left ventricular wall motion abnormalities. Those having received propranolol within 48 hr of angiography or with contraindications to administration of propranolol were excluded, as were those with any valvular lesions. Informed consent was obtained from all patients prior to study.

Fifteen males and one female, with ages ranging from 34 to 61 years with a mean age of 47 were studied. An initial group of eight patients was studied using an intravenous propranolol dose of 0.10 mg/kg. When it became apparent that this dose resulted in no deleterious effects and no significant changes in left ventricular wall motion, the dose was increased to 0.15 mg/kg for the second group of eight patients.

Coronary angiography, using either a brachial arterial or percutaneous femoral arterial approach, was performed initially in all studies since this was of greatest diagnostic importance. Thirty minutes following the last coronary injection, left ventricular and radial arterial pressures were recorded and cardiac output was determined using the Fick method. Left ventricular cineangiography was then performed in held mid-inspiration, being certain that a Valsalva maneuver was not performed, with injection of 40–60 cc of sodium meglumine diatrizoate (Renografin-76), at a rate of 15–20 cc/sec with the patient in a 30° right anterior oblique (RAO) position, using 35 mm film at 60 frames/sec. Immediately following ventriculography, left ventricular and radial arterial pressures were measured. Twenty to 30 minutes later, pressures and cardiac output were again determined. Propranolol was then administered intravenously in a dose of either 0.10 or 0.15 mg/kg at a rate of approximately 1 mg/min. Twenty minutes later, pressures and cardiac output were again measured and left ventricular angiography repeated. Pressures were recorded again immediately after ventriculography. Care was taken that the position of the patient was not changed between the two angiograms and that the same technique was used for both. Right atrial or coronary sinus pacing at a rate slightly greater than the sinus rate was employed throughout the study to avoid the effects of rate changes on ventricular function.

Ejection fraction (EF) was determined from the single plane RAO angiograms using planimetry and the method described by Sandler and Dodge[4] as applied to the RAO projection with appropriate correction for roentgenographic magnification. End-systolic and end-diastolic frames were selected for analysis from the earliest beat following ventricular opacification and at least two beats following any ectopic beats. For determination of wall motion, projected images of these frames were superimposed by tracing their outlines, including papillary muscles, without moving the paper on which they were traced, ascertaining that diaphragmatic or chest wall movement had not occurred between systole and diastole. Each film was also evaluated subjectively from the projected moving cineangiograms by each of the investigators.

## Results

Results of coronary and left ventricular angiography are shown in table 1. All but four patients had significant obstructive coronary artery disease; of these four, one had no apparent cardiac disease (R.MG.) and the other three (W.W., S.L., D.P.) were felt to have a cardiomyopathy on the basis of clinical presentation and hemodynamic and angiographic evidence of left ventricular dysfunction.

Of the patients with significant coronary lesions, all but one (R.M.) had abnormalities of left ventricular wall motion (LVWM) corresponding to the distribution of obstructed vessels (table 1 and figs. 1, 2). Three patients (G.F., J.C., H.E.) had additional apparent slight anterior hypokinesis without significant lesions of the left anterior descending artery (LAD). Two patients (L.A., J.M.) were excluded from analysis of LVWM because of inadequate ventriculograms; the hemodynamic responses of these patients, however, are included.

Propranolol resulted in no detectable change in LVWM in nine out of 14 patients analyzed. At a dosage of 0.10 mg/kg, a minimal diffuse increase in hypokinesis occurred in only one patient (J.C.). At the higher dose of 0.15 mg/kg, a very slight increase in

**Table 1**

*Coronary Anatomy and Left Ventricular Regional Contractility Before and After Propranolol*

| Patient | % Coronary obstruction RCA | LAD | LCF | Regional contractility Pre-propranolol | Post-propranolol |
|---|---|---|---|---|---|
| | | | | *0.10 mg/kg Propranolol* | |
| W.W. | 0 | 0 | 0 | Diffuse hypo | No change |
| A.P. | 100 | 70* | 100 | Antero-apical hypo | No change |
| G.F. | 100 | 0 | 0 | Inferior akin, slight apical dysk, anterior hypo | No change |
| J.S. | 100 | 0* | 50 | Inferior akin, apical dysk, anterior hypo | No change |
| J.C. | 100 | 0 | 70 | Moderate diffuse hypo | Slight diffuse worsening |
| R.MG. | 0 | 0 | 0 | Normal | No change |
| L.A. | 100 | 100 | 100 | — | — |
| J.M. | 100 | 90 | 100 | — | — |
| | | | | *0.15 mg/kg Propranolol* | |
| R.M. | 50 | 0 | 100 | Normal | No change |
| D.G. | 70 | 90 | 0 | Diffuse severe hypo, apical akin | No change |
| E.B. | 100 | 0 | 100 | Inferior akin, slight apical dysk | No change |
| P.D. | 90 | 80 | 70 | Inferior akin, slight anterior hypo | No change |
| S.L. | 0 | 0 | 0 | Slight anterior hypo | New inferior hypo |
| A.M. | 90 | 0* | 90 | Inferior akin and slight dysk | New slight anterior hypo |
| H.E. | 70 | 0 | 100 | Anterior-inferior hypo, apical akin | New slight apical dysk; slight increase; anterior hypo |
| D.P. | 0 | 0 | 0 | Antero-apical akin, slight apical dysk | New slight inferior hypo |

*Patients with significant obstruction of the LAD diagonal branch.

Abbreviations: LAD = left anterior descending coronary artery; LCF = left circumflex coronary artery; RCA = right coronary artery; hypo = hypokinesis; akin = akinesis; dysk = dyskinesis.

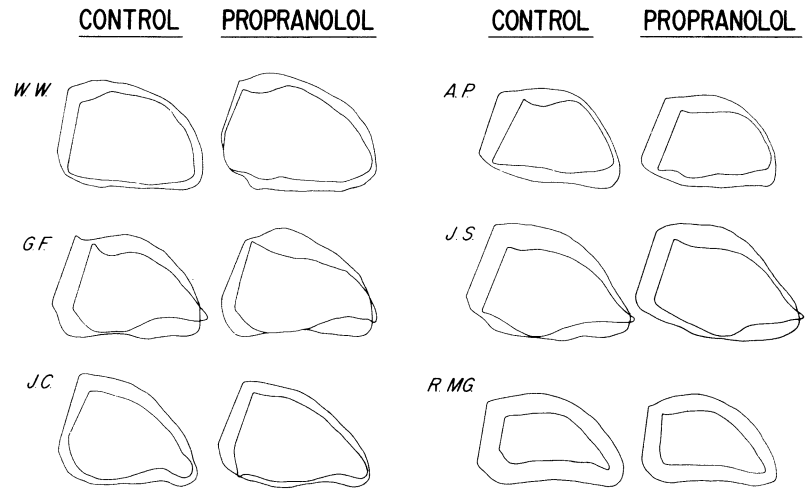


**Figure 1**

*Left ventricular wall motion in six patients before and after intravenous propranolol 0.10 mg/kg.*

anterior hypokinesis and an equivocal appearance of apical dyskinesis occurred in one patient (H.E.) with an occluded LCF and RCA disease, who had diffuse hypokinesis and apical akinesis initially. New slight hypokinesis occurred in two patients, one (A.M.) with RCA, LCF and LAD diagonal branch disease having initial inferior wall akinesis and apical hypokinesis who developed slight anterior hypokinesis after propranolol, and another (D.P.) with normal coronary arteries and initial antero-apical akinesis who developed equivocal new inferior wall hypokinesis. Another patient (S.L.) with normal coronary arteries and initially only slight anterior hypokinesis developed new inferior wall hypokinesis after propranolol. The authors in addition carefully reviewed all of the angiograms without observing the traced outlines and, except for the readily apparent change in inferior wall motion in patient S.L., could detect no effect of propranolol on wall motion abnormalities. Indeed, the slight changes which were demonstrated by superimposing tracings were all sufficiently small that it is unlikely they would be subjectively apparent.

Changes in ejection fraction (EF) (table 2) correlate well with changes observed in LVWM in the patients with coronary artery disease. In two patients without

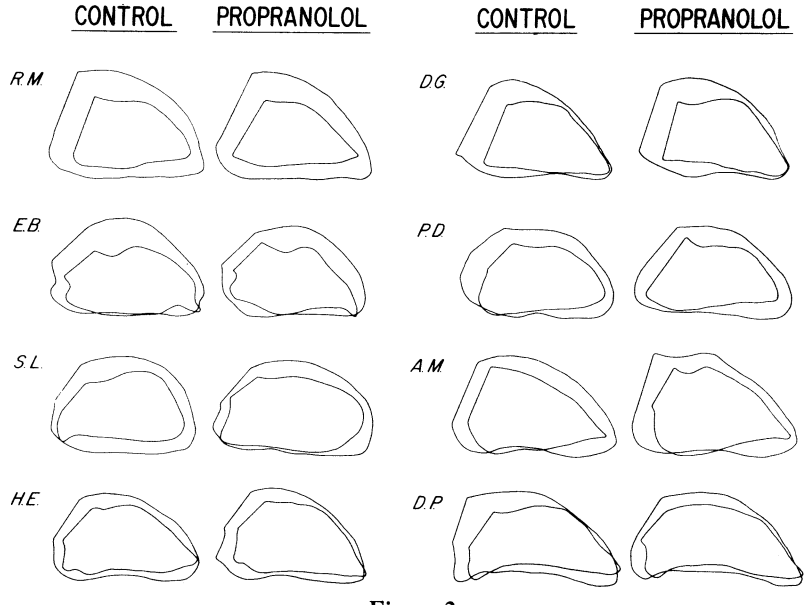


**Figure 2**

*Left ventricular wall motion in eight patients before and after intravenous propranolol 0.15 mg/kg.*

**Table 2**

*Effects of Propranolol on Left Ventricular Hemodynamics*

| Patient | LV end-diastolic pressure (mm Hg) | | | | | LV systolic pressure (mm Hg) | | | | | CI (L/min/m²) | | EF | | EDV (cc/m²) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cont | Cont angio | Pre-prop | Post-prop | Prop angio | Cont | Cont angio | Pre-prop | Post-prop | Prop angio | Pre-prop | Post prop | Pre-prop | Post-prop | Pre-prop | Post-prop |
| *0.10 mg/kg Propranolol* | | | | | | | | | | | | | | | | |
| W.W. | 5 | 10 | 3 | 5 | 12 | 135 | 150 | 140 | 125 | 150 | 2.1 | 2.6 | .37 | .24 | 121 | 139 |
| A.P. | 7.5 | 19 | 5 | 9 | 20 | 146 | 168 | 160 | 168 | 165 | 2.4 | 2.6 | .57 | .58 | 78 | 70 |
| G.F. | 14 | — | 18 | 15 | 14 | 143 | 100 | 148 | 145 | 100 | 3.2 | — | .58 | .53 | 105 | 98 |
| J.S. | 13.5 | 20 | 13 | 14 | 22 | 142 | 135 | 135 | 140 | 150 | 3.6 | 3.1 | .58 | .54 | 110 | 109 |
| J.C. | 15 | 20 | 13 | 10 | 22 | 140 | 148 | 138 | 140 | 140 | 3.4 | 2.4 | .50 | .42 | 78 | 104 |
| R.MG. | 3 | 10 | 4 | 3 | 9 | 136 | — | 136 | — | — | 2.9 | 3.3 | .79 | .70 | 70 | 65 |
| L.A. | 11 | 35 | 10 | 10 | 33 | 148 | 156 | 134 | 148 | 136 | 2.4 | 2.7 | — | — | — | — |
| J.M. | 9 | 25 | 14 | 12 | 18 | 103 | 118 | 103 | 103 | 92 | 3.5 | 3.0 | — | — | — | — |
| Mean | 9 | 20 | 10 | 9 | 19 | 137 | 139 | 137 | 138 | 133 | 2.9 | 2.8 | .57 | .50* | 98 | 104 |
| SEM | 2 | 3 | 2 | 2 | 3 | 5 | 9 | 6 | 8 | 10 | 0.2 | 0.1 | .06 | .06 | 9 | 11 |
| *0.15 mg/kg Propranolol* | | | | | | | | | | | | | | | | |
| R.M. | 10 | 17 | 15 | 11 | 14 | 115 | 118 | 115 | 115 | 107 | 4.3 | 3.0 | .69 | .74 | 126 | 105 |
| D.G. | 12 | 20 | 13 | 13 | 20 | 133 | 132 | 138 | 140 | 132 | 3.9 | 2.9 | .53 | .57 | 93 | 104 |
| E.B. | 9 | 14 | 10 | 5 | 13 | 160 | 175 | 160 | 150 | 160 | 2.7 | 2.3 | .59 | .58 | 113 | 110 |
| P.D. | 3 | 15 | 2 | 4 | 18 | 146 | 142 | 148 | 140 | 116 | 2.8 | 2.4 | .52 | .57 | 101 | 95 |
| S.L. | 10 | 16 | 9 | 9 | 12 | 140 | 127 | 130 | 132 | 130 | 2.9 | 2.1 | .59 | .41 | 106 | 99 |
| A.M. | 8 | 13 | 8 | 7 | 14 | 145 | 160 | 155 | 160 | 170 | 4.4 | 3.3 | .53 | .50 | 108 | 116 |
| H.E. | 2 | 8 | 3 | 6 | 8 | 140 | 150 | 145 | 150 | 150 | 2.9 | 2.6 | .51 | .47 | 78 | 89 |
| D.P. | — | 4 | 2 | 2 | 4 | — | 140 | 125 | 125 | 130 | 3.4 | 2.5 | .53 | .45 | 88 | 81 |
| Mean | 8 | 13 | 8 | 7 | 13 | 140 | 143 | 140 | 139 | 134 | 3.4 | 2.6* | .56 | .54 | 104 | 103 |
| SEM | 1 | 2 | 2 | 1 | 2 | 5 | 7 | 6 | 5 | 8 | 0.2 | 0.1 | .02 | .04 | 6 | 3 |

*$P < .05$.

Abbreviations: LV = left ventricular; CI = cardiac index; EDV = end-diastolic volume; cont = control; prop = propranolol; cont angio = values immediately post-control ventriculogram; prop angio = values immediately post-propranolol ventriculogram.



coronary artery disease (W.W. and R.MG) there was a reduction in EF without a detectable change in LVWM. Of the five patients with a detectable worsening of LVWM, EF fell by more than 5% in four, the greatest decrease of 18% occurring in the patient (S.L.) with obvious development of inferior wall hypokinesis. EF for the entire group of patients did not change significantly following propranolol.

At the dose of 0.10 mg/kg, cardiac index measured by the Fick method before and after propranolol changed variably without any significant change for the group (table 2). At the higher dose of 0.15 mg/kg cardiac index consistently fell, from a mean of $3.4 \pm 0.2$ to $2.6 \pm 0.1$ L/min/m² ($P < 0.001$). Since heart rate was maintained unchanged by atrial pacing, stroke volume changed similarly. Stroke volumes determined angiographically showed changes qualitatively similar to those obtained by the Fick method in the majority of cases, although several marked inconsistencies were apparent (patients W.W., R.MG., D.G., A.M.). Changes in end-diastolic volume determined angiographically were variable and not statistically significant (table 2). Left ventricular end-systolic and end-diastolic pressures measured before and after propranolol did not change significantly (table 2). Similarly, pressures recorded immediately following the initial ventriculogram were not significantly different from those recorded immediately after the propranolol ventriculogram. No patient exhibited any clinical deterioration following administration of propranolol at these doses.

## Discussion

In 1971, Helfant et al. reported, in a group of ten patients, four of whom had coronary artery disease, that 5 mg of propranolol given intravenously resulted in the appearance of new or increased left ventricular asynergy.[3] Three out of four patients with coronary disease developed such changes with new occurrence of hypokinesis in one and increased asynergy resulting in akinesis and dyskinesis in two others. Furthermore, of those with normal coronary arteries, one patient was reported to have developed hypokinesis and another patient dyskinesis. No subsequent angiographic studies have been reported to confirm these findings. Using radarkymographic video tracking techniques, Ludbrook et al.[2] demonstrated, to the contrary, that the same dose of propranolol resulted in decreased amplitude of movement in dyskinetic as well as in normal and hypokinetic segments; in no case was paradoxical systolic outward bulging accentuated nor did new areas of dyskinesis appear after propranolol. Our data indicate that considerably larger doses of propranolol resulted in no significant

changes in left ventricular wall motion in the majority of patients with a wide spectrum of coronary lesions and wall motion abnormalities. Minimal worsening of previously hypokinetic areas was detectable in two patients and new areas of slight hypokinesis could be demonstrated in two other patients. Only one new area of hypokinesis, in a patient with a cardiomyopathy and normal coronary arteries, could be appreciated by subjective visual review of the cineangiograms.

Several methods have been employed for superimposing diastolic and systolic left ventricular outlines for purposes of evaluating wall motion, although there remains considerable controversy concerning which is most valid. Helfant et al., in their study of the effects of propranolol on wall motion,[3] superimposed the long axes and the midpoints of the aortic valve of the end-diastolic and end-systolic frames, a method also reported in other studies.[5-7] This assumes that the long axis does not change during systolic contraction and that the left ventricular wall contracts symmetrically toward the base of the heart, the latter assumption in particular being incorrect since the aortic valve has been shown to move toward the apex in systole.[8] Other investigators[1, 9] have used the method of superimposing the long axis and an axis perpendicularly bisecting the long axis, thereby implying symmetrical contraction toward the approximate center of the ventricle. This also is unlikely to be correct in a ventricle with asynergy. In any case, an asynergic heart will not usually contract symmetrically about the long axis, and only slight changes in selection of a long axis (which may be very difficult to define in such an asynergic ventricle) may cause superimposition of these axes to result in false appearance or disappearance of wall motion abnormalities. Since the heart moves minimally in the chest during contraction, providing there is no diaphragmatic movement and that neither the patient nor the table is moved[10, 11] it has been suggested that superimposition of fixed external reference markers, i.e., chest structures or lead markers, may permit more accurate evaluation of wall motion.[11, 12] This method has been reported to more reliably detect areas of asynergy in patients with coronary artery disease.[11] However, no one of these reference systems appears to be uniformly valid in evaluating changes during systolic contraction and further investigations in this area are needed.

In the present study, we superimposed ventricular outlines using the diaphragm and ribs as fixed references, being certain that no diaphragmatic or table movement had occurred. It was apparent that wall motion evaluated in this manner agreed with subjective visual interpretation of the cineangiogram and with location of coronary artery lesions. Since exactly the same technique and position was used for angiography before and after propranolol, any errors resulting from methods of superimposition should have minimal effect on interpretation of the effect of propranolol. Although angiography was performed in only a single plane, use of the right anterior oblique projection permits adequate evaluation of all segments except for the true posterior wall and septum. Injection of contrast material by the technique used in this study has been demonstrated not to affect left ventricular size or contractility within the first five beats after ventricular injection[13] or after 20 to 30 minutes following either coronary or left ventricular angiography.[13]

Propranolol has been reported to significantly reduce angina and improve exercise tolerance in patients with coronary disease[14-17] although not all studies have confirmed these findings.[18, 19] Cardiac index, left ventricular dp/dt, left ventricular work index and systolic ejection rate have been shown to be decreased significantly following intravenous propranolol,[20-22] but it has been suggested that the over-all effect is a reduction in myocardial oxygen consumption[23] resulting in an improvement in myocardial oxygenation and left ventricular function.[24]

Our data indicate that even with the large doses of propranolol used, left ventricular end-diastolic pressure at rest did not change significantly from control either before or after ventriculography. A significant decrease in cardiac index measured by the Fick method with unchanged heart rate occurred at the higher propranolol dosage only. The difference between changes in stroke volume determined by the Fick and angiographic methods is probably the known unreliability of ventricular volumes calculated from the single plane angiogram in patients with coronary artery disease and ventricular wall asynergy.[25] However the discrepancies between the Fick and angiographic methods do not affect the validity of the observation in the present study that propranolol produces only minimal changes in segmental wall motion during single plane ventriculography when cardiac position and heart rate are kept constant.

Propranolol in a dosage of 0.15 mg/kg has been shown to block about three-fourths of exercise-induced tachycardia and to increase by approximately 25 times the dose of isoproterenol required to produce a given increase in heart rate, the peak such effect observed 15 minutes after intravenous administration.[26] Plasma propranolol levels during oral administration vary considerably, with chronic oral dosages of 160–320 mg/day being required to achieve plasma levels equivalent to those occurring 15

minutes following intravenous infusion of 0.15 mg/kg.[26, 27] Although studies have been limited, similar plasma propranolol levels achieved by either the intravenous route or with chronic oral administration have been demonstrated to result in similar degrees of beta-adrenergic blockade.[28] Certainly, propranolol in doses sufficiently large to have considerable beta-blocking effect resulted in no significant effect on left ventricular end-diastolic pressure and, in nearly all cases, no or minimal effects on wall motion. The only patient (S.L.) showing a large decrease in ejection fraction and noticeable worsening of wall motion was one with normal coronary arteries and a cardiomyopathy without typical angina, who would be unlikely to be treated with propranolol. As previously discussed, chronic oral administration could possibly have a somewhat different effect, and clinical evaluation is, of course, necessary. Our data would indicate that even relatively large doses of propranolol may be used without serious detrimental effects at rest in patients with coronary disease, including those having significant wall motion abnormalities.

## References


1. Hamilton GW, Murray JA, Kennedy JW: Quantitative angiocardiography in ischemic heart disease. Circulation **45:** 1065, 1972
2. Ludbrook P, Karliner JS, Kostuk W, O'Rourke RA: Effects of intravenously administered propranolol on wall motion abnormalities. Am J Cardiol **31:** 712, 1973
3. Helfant RH, Herman MV, Gorlin R: Abnormalities of left ventricular contraction induced by beta adrenergic blockade. Circulation **43:** 641, 1971
4. Sandler H, Dodge HT: The use of single plane angiocardiograms for the calculation of left ventricular volume in man. Am Heart J **75:** 325, 1968
5. Herman MV, Heinle RA, Klein MD, Gorlin R: Localized disorders in myocardial contraction. N Engl J Med **277:** 222, 1967
6. Rees G, Bristow JD, Kremakau EL, Green GS, Herr RH, Griswald HE, Starr A: Influence of aortocoronary bypass on left ventricular performance. N Engl J Med **284:** 1116, 1971
7. Klein MD, Herman M, Gorlin R: A hemodynamic study of left ventricular aneurysm. Circulation **35:** 614, 1967
8. McDonald IG: The shape and movements of the human left ventricle during systole. Am J Cardiol **26:** 221, 1970
9. Chatterjee K, Swan HJC, Parmley WW, Sustaita H, Marcus HS, Matloff J: Influence of direct myocardial revascularization on left ventricular asynergy and function in patients with coronary heart disease. Circulation **47:** 276, 1973
10. Dodge HT, Sandler H, Baxley WA, Hawley RR: Usefulness and limitations of radiographic methods for determining left ventricular volume. Am J Cardiol **18:** 10, 1966
11. Chaitman BR, Bristow JD, Rahimtoola SH: Left ventricular wall motion assessed by using fixed external reference system. Circulation **48:** 1043, 1973
12. Kitamura S, Kay JH, Krohn BG, Magidson O, Dunne EF: Geometric and functional abnormalities of the left ventricle with a chronic localized noncontractile area. Am J Cardiol **31:** 701, 1973
13. Hammermeister KE, Warbasse JR: Immediate hemodynamic effects of cardiac angiography in man. Am J Cardiol **31:** 307, 1973
14. Gianelly RE, Goldman RH, Treister B, Harrison DC: Propranolol in patients with angina pectoris. Ann Intern Med **67:** 1216, 1967
15. Gianelly RE, Treister BL, Harrison DC: The effect of propranolol on exercise-induced ischemic ST segment depression. Am J Cardiol **24:** 161, 1969
16. Dagenais GR, Pitt B, Ross RS: Exercise tolerance in patients with angina pectoris. Am J Cardiol **28:** 10, 1971
17. Grant RHE, Keelan P, Kernohan RJ, Leonard JC, Nancekievill L, Sinclair K: Multicenter trial of propranolol in angina pectoris. Am J Cardiol **18:** 361, 1966
18. Aronow WS, Kaplan MA: Propranolol combined with isosorbide dinitrate versus placebo in angina pectoris. N Engl J Med **280:** 847, 1969
19. Aronow WS: The medical treatment of angina pectoris. VI. Propranolol as an antianginal drug. Am Heart J **84:** 706, 1972
20. Hamer J, Sowton E: Cardiac output after beta-adrenergic blockade in ischemic heart disease. Br Heart J **27:** 892, 1965
21. Weiner L, Dwyer EM, Cox JW: Hemodynamic effects of nitroglycerine, propranolol and their combination in coronary heart disease. Circulation **39:** 623, 1969
22. Parker JO, West RO, DiGiorgi S: Hemodynamic effects of propranolol in coronary artery disease. Am J Cardiol **26:** 11, 1968
23. Wolfson S, Heinle RA, Herman MM MV: Propranolol and angina pectoris. Am J Cardiol **18:** 345, 1966
24. Maroko PR, Libby P, Braunwald E: Effect of pharmacologic agents on the function of the ischemic heart. Am J Cardiol **32:** 930, 1973
25. Cohn PF, Gorlin R, Adams DF, Chahine RA, Vokonas PS, Herman MV: Comparison of biplane and single plane left ventriculograms in patients with coronary artery disease. Am J Cardiol **33:** 1, 1974
26. Coltart DG, Shand DG: Plasma propranolol levels in the quantitative assessment of beta adrenergic blockade in man. Br Med J **3:** 731, 1970
27. Evans GH, Shand DG: Disposition of propranolol: Drug accumulation and steady state concentration during chronic oral administration in man. Clin Pharmacol Ther **14:** 48, 1973